

CLAIMS

1. A method for reacting a reagent R with at least one cell C, said method being characterized in that:
 - 5 - the cell C is deposited on a support S comprising a substantially flat surface, in the form of an aqueous drop on said surface;
 - 10 - the substantially flat surface of the support S on which the aqueous drop containing the cell C has been deposited is covered with a separation film F, allowing gases to pass through and preventing evaporation of the aqueous drops deposited on the support S, F being non-miscible with the reagent R;
 - 15 - the reaction between the reagent R and the cell C is triggered by introducing the reagent R into the aqueous drop containing the cell C.
- 20 2. The method as claimed in claim 1, characterized in that the drops are attached to the support S by capillarity.
- 25 3. The method as claimed in claim 1 or claim 2, characterized in that the support S consists of a plate made of a material chosen from silicon, glass or a polymer.
- 30 4. The method as claimed in any one of claims 1 to 3, characterized in that the support S has, on its flat surface, at least one means intended for the reception of the aqueous drops.
- 35 5. The method as claimed in any one of claims 1 to 4, characterized in that an aqueous drop containing the cell C is deposited on the support S, a second aqueous drop containing the reagent R is injected, using any

appropriate injection means, directly into the drop containing the cell C.

6. The method as claimed in any one of claims 1 to 4,
5 characterized in that a first aqueous drop is deposited on the support S and then a second aqueous drop is deposited on the same support in the vicinity of the first one of these drops contains the cell C, the other 10 reagent R, and the reaction of the reagent R with the cell C is triggered by the fusion of the two drops.

7. The method as claimed in any one of claims 1 to 4, characterized in that the reagent R is attached to the support S or to the film F, the cell C is deposited in 15 the form of an aqueous drop on the support S and the reagent R is then detached from the support S or from the film F in order to allow it to react with the cell.

8. The method as claimed in any one of Claims 1 to 7,
20 characterized in that the separation film F is a liquid chosen from oils and organic solvents.

9. The method as claimed in claim 8, characterized in that the separation film F is chosen from mineral oils 25 and silicone oils.

10. The method as claimed in any one of claims 1 to 7, characterized in that the separation film F is air saturated with moisture.

30 11. The method as claimed in one of claims 1 to 7, characterized in that the separation film F is a flexible, solid film.

35 12. The method as claimed in claim 11, characterized in that the separation film F is made of polydimethylsiloxane or of nitrocellulose.

13. The method as claimed in any one of claims 1 to 7,

characterized in that the separation film F is a rigid honeycombed cover made of porous material.

5 14. The method as claimed in any one of claims 1 to 13, characterized in that the aqueous drops containing one or more cells or a reagent are deposited on the support S by means of fine capillaries.

10 15. The method as claimed in any one of claims 1 to 13, characterized in that the aqueous drops containing one or more cells or a reagent are deposited on the support S by means of a nozzle.

15 16. The method as claimed in any one of claims 1 to 15, characterized in that it comprises a step for displacing the support S after the first series of drops has been deposited on the support S.

20 17. The method as claimed in any one of claims 1 to 16, characterized in that the cell cultures in the form of aqueous drops are conserved for at least 24 hours.

25 18. The method as claimed in any one of claims 1 to 17, characterized in that several aqueous drops each comprising at least one cell are deposited on the support S, under the separation film F, said drops being isolated from one another.

30 19. The method as claimed in any one of claims 1 to 18, characterized in that a drop contains from 1 to 100 cells.

35 20. The method as claimed in either one of claims 18 and 19, characterized in that different cells are placed in the various drops.

21. The method as claimed in either one of claims 18 and 19, characterized in that identical cells are placed in the various drops.

22. The method as claimed in claim 21, characterized in that the support is a hydrophobic plate comprising hydrophilic zones and in that the step for injecting the aqueous drops containing cells is replaced with the 5 immersion of the plate in an aqueous solution containing the cells.

23. The method as claimed in any one of claims 1 to 10 22, characterized in that the reagent molecules are prepared directly after depositing on the support, by means of a method chosen from *in situ* synthesis, *in vitro* transcription in the drop, peptide polymerase chain reaction and nucleic acid polymerase chain reaction.

15 24. The method as claimed in any one of claims 1 to 23, characterized in that the reagent is a DNA molecule.

20 25. The method as claimed in claim 24, characterized in that the DNA is in a form that has been precipitated, in particular in the form of calcium phosphate.

25 26. The method as claimed in any one of claims 1 to 23, characterized in that the reagent is a transcription factor.

30 27. The method as claimed in any one of claims 1 to 26, characterized in that several reagents intended to react with the same cell are deposited successively.

35 28. The method as claimed in any one of claims 1 to 27, characterized in that several aqueous drops containing cells are deposited and these drops are fused.

29. The method as claimed in claim 28, characterized in that glial cells and neurons are deposited so as to

make them communicate within the same drop.

30. The method as claimed in any one of claims 1 to
29, characterized in that reagents are reacted in a
5 first cell type so as to trigger a cellular reaction,
such as the production of a recombinant protein, and
then this first cell is reacted with a cell of another
type, by fusion with another drop.

10 31. The method as claimed in any one of claims 1 to
30, in which the support comprises separation means,
characterized in that an aqueous drop comprising at
least one cell of a first type is deposited on one side
of the separation means and an aqueous drop comprising
15 at least one cell of a second type is deposited on the
other side of the separation means, and then in that
the cell drops are fused.

20 32. The method as claimed in any one of claims 1 to
31, characterized in that the reagent is chosen from
labeled molecules, in particular fluorescent radio-
active labels.

25 33. The method as claimed in any one of claims 1 to
32, characterized in that the cell is chosen from:
primary cells, hybridomas, cell lines, stem cells, a
piece of cell tissue, and mixtures thereof.

30 34. A device for reacting a reagent R with a cell C,
this device being characterized in that it comprises:

35 - a support S comprising a substantially flat
surface covered with a separation film F allowing
gases to pass through and preventing the
evaporation of the aqueous drops deposited on the
support S, F being non-miscible with the reagent
R,

- means for depositing, on said surface and under

the film F, aqueous drops containing the cell C,

- a controlled-atmosphere chamber in which the support S is placed so as to allow the cell C to
5 survive.

35. The device as claimed in claim 34, characterized in that the support S consists of a plate made of a material chosen from silicon, glass or a polymer.

10 36. The device as claimed in either one of claims 34 and 35, characterized in that the support S has, on its flat surface, at least one means intended for the reception of the aqueous drops.

15 37. The device as claimed in claim 36, characterized in that the means intended for the reception of the aqueous drops consists of zones of the flat surface of the support S that range from $5 \mu\text{m}^2$ to 5 mm^2 in size.

20 38. The device as claimed in claim 36 or claim 37, characterized in that the support S has at least one of the characteristics a) to d) below:

25 a) the support S exhibits on its flat surface a hydrophobic nature, and comprises one or more hydrophilic zones constituting the reception means;

30 b) the support S comprises, on its flat surface, cavities ranging from 1 micron to 1 millimeter in depth, constituting the reception means;

35 c) the support S is a plate equipped with outgrowths ranging from 1 micron to 1 millimeter in thickness, arranged on its surface and intended to promote the attachment of the drops;

d) the support S is a plate equipped with at least one wire, to which the drops attach.

39. The device as claimed in claim 38, in which the support S exhibits on its flat surface a hydrophobic nature, and comprises one or more hydrophilic zones, characterized in that it also comprises a second means 5 for receiving the drops, superimposed on the first.

40. The device as claimed in any one of claims 34 to 39, characterized in that the means for depositing the aqueous drops on the support S consist of fine 10 capillaries.

41. The device as claimed in any one of claims 34 to 40, characterized in that the means for depositing the aqueous drops on the support S consist of a 15 piezoelectric system equipped with a nozzle.

42. The device as claimed in any one of claims 34 to 41, characterized in that the support S of the device is mobile.

20 43. The device as claimed in any one of claims 34 to 42, characterized in that the support S consists of a solid film attached to rollers at its two ends, the rollers being equipped with winding means so as to 25 allow displacement of the film and therefore displacement of the drops which have been deposited on it.

44. The device as claimed in any one of claims 34 to 30 43, characterized in that it also comprises at least one means chosen from:

- means for supplying energy to one or more drops deposited on the support;
- 35 - means for optical treatment of one or more drops deposited on the support;
- means for applying a magnetic field or an electric

field to one or more drops deposited on the support;

- means of detection focused on one or more drops deposited on the support;

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- means intended to promote transfection.

45. The device as claimed in any one of claims 34 to 44, characterized in that the means used in the device 10 are connected to a control device making it possible to automate it.

46. The device as claimed in any one of claims 34 to 45, characterized in that the support comprises 15 reception means arranged evenly in the form of matrices.

47. The device as claimed in any one of claims 33 to 45, characterized in that the support is equipped with 20 separation means that make it possible to separate two different cell types but that permit the passage of small molecules between these cells.

48. The device as claimed in claim 47, characterized 25 in that the separation means are arranged on the reception means, on the support.

49. The device as claimed in any one of claims 34 to 48, characterized in that the aqueous drops containing 30 one or more cells comprise a culture medium.

50. The device as claimed in any one of claims 34 to 49, characterized in that the support has a surface 35 whose hydrophilicity/hydrophobicity properties may vary under the influence of a parameter such as the temperature, and a electric field, a magnetic field or an irradiation.

51. The use of a device as claimed in any one of

claims 34 to 50, for carrying out, simultaneously and in an automated manner, a large number of reactions of a reagent on a cell, varying the nature of the reagent and of the cell.

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52. The use as claimed in claim 51, for carrying out the screening of a set of chemical compounds on living cells.

10 53. The use of a device as claimed in any one of claims 34 to 50, for studying cell systems chosen from: neuronal networks and the epidermis.

15 54. The use of a device as claimed in any one of claims 34 to 50, for studying the action, on a cell, of a reagent chosen from: nucleic acid molecules, proteins, peptides and peptide nucleic acid molecules.

20 55. The use of a device as claimed in any one of claims 34 to 50, for expressing recombinant proteins.

25 56. The use of a device as claimed in any one of claims 34 to 50, for screening nucleic acid molecules intended to modify gene expression in cells.

57. The use of a device as claimed in any one of claims 34 to 50, for searching for promoter genomic sequences.

30 58. The use of a device as claimed in any one of claims 34 to 50, for studying the interactions between cells of various types.

35 59. The use of a device as claimed in any one of claims 34 to 50, for preparing and screening siRNA.